

General

Guideline Title

Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline.

Bibliographic Source(s)

The Endocrine Society. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. Chevy Chase (MD): The Endocrine Society; 2012. 99 p. [387 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: The Endocrine Society. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. Chevy Chase (MD): The Endocrine Society; 2007. 79 p.

Recommendations

Major Recommendations

Definitions for the quality of the evidence based on the United States Preventative Services Task Force (USPSTF) levels (good, fair, and poor) and Grading of Recommendations Assessment, Development and Evaluation (GRADE) levels (+OOO, ++OO, +++O, and ++++) and the strength of the recommendation (USPSTF: A, B, C, D, I and GRADE: 1 or 2) are provided at the end of the "Major Recommendations" field.

Management of Hypothyroidism: Maternal and Fetal Aspects

The task force recommends caution in the interpretation of serum free thyroxine (T_4) levels during pregnancy and that each laboratory establish trimester-specific reference ranges for pregnant women if using a free T_4 assay. The non-pregnant total T_4 range (5–12 $\mu\text{g/dL}$ or 50–150 nmol/L) can be adapted in the second and third trimesters by multiplying this range by one and a half-fold. Alternatively, the free thyroxine index ("adjusted T_4 ") appears to be a reliable assay during pregnancy. (USPTF Recommendation level: B, Evidence-fair) (2|++OO)

Overt maternal hypothyroidism is known to have serious adverse effects on the fetus. Therefore maternal hypothyroidism should be avoided. For overt hypothyroidism: (USPSTF Recommendation level: A, Evidence-good) (1|+++O)

Subclinical hypothyroidism (SCH; serum thyroid-stimulating hormone [TSH] concentration above the upper limit of the trimester-specific reference range with a normal free T_4) may be associated with an adverse outcome for both the mother and offspring, as documented in antibody-positive women. In retrospective studies thyroxine treatment improved obstetrical outcome, but it has not been proved to modify long-term neurological development in the offspring. However, given that the potential benefits outweigh the potential risks, the panel recommends thyroxine replacement in women with SCH who are thyroid peroxidase antibody positive (TPO-Ab+). For obstetrical outcome: (USPSTF Recommendation level: B,

Evidence-fair) (2|++OO); for neurological outcome: (USPSTF Recommendation level: I, Evidence-poor) (2|OOOO). The panel also recommends thyroxine replacement in women with SCH who are TPO-Ab-. For obstetrical outcome: (USPSTF Recommendation level: C, Evidence-fair) (2|++OO); for neurological outcome: (USPSTF Recommendation level: I, Evidence-poor) (2|OOOO)

If hypothyroidism has been diagnosed before pregnancy, the task force recommends adjustment of the preconception thyroxine dose to reach prior to pregnancy a TSH level not higher than 2.5 mIU/L. (USPSTF Recommendation level: C, Evidence-poor) (2|+OOO)

The thyroxine dose usually needs to be incremented by four to six weeks gestation and may require a 30% or more increase in dosage. (USPSTF Recommendation level: A, Evidence-good) (1|++++)

If overt hypothyroidism is diagnosed during pregnancy, thyroid function tests should be normalized as rapidly as possible. Thyroxine dosage should be titrated to rapidly reach and thereafter maintain serum TSH concentrations of less than 2.5 mIU/L (in an assay using the International Standard) in the first trimester (or 3 mIU/L in second and third trimester) or to trimester-specific TSH ranges. Thyroid function tests should be remeasured within 30–40 days and then every four to six weeks. (USPSTF Recommendation level: A, Evidence-good) (1|++++)

Women with thyroid autoimmunity who are euthyroid in the early stages of pregnancy are at risk of developing hypothyroidism and should be monitored every four to six weeks for elevation of TSH above the normal range for pregnancy. (USPSTF Recommendation level: A, Evidence-fair) (1|+++O)

After delivery, most hypothyroid women need to decrease the thyroxine dosage they received during pregnancy to the pre-pregnancy dose. (USPSTF Recommendation level: A, Evidence-good) (1|++++)

Management of Hyperthyroidism: Maternal and Fetal Aspects

Management of Maternal Hyperthyroidism: Maternal Aspects

If a subnormal serum TSH concentration is detected during gestation, hyperthyroidism must be distinguished from both normal physiology of pregnancy and gestational thyrotoxicosis because of the adverse effects of overt hyperthyroidism on the mother and fetus. Differentiation of Graves' disease from gestational thyrotoxicosis is supported by presence of clinical evidence of autoimmunity, a typical goiter, and presence of thyrotropin receptor antibodies (TRAb). TPO-Ab may be present in either case. (USPSTF Recommendation level: B, Evidence-fair) (1|+++O)

For overt hyperthyroidism due to Graves' disease or thyroid nodules, antithyroid drug (ATD) therapy should be either initiated (before pregnancy if possible, and for those with new diagnoses) or adjusted (for those with a prior history) to maintain the maternal thyroid hormone levels for free T₄ at or just above the upper limit of the non-pregnant reference range (USPSTF Recommendation level: B, Evidence-fair) (1|++OO) or maintaining total T₄ at one and a half times the upper limit of the normal reference range, or the free thyroxine index in the upper limit of the normal reference range. (USPSTF Recommendation level: I, Evidence-poor) (2|+OOO)

Propylthiouracil (PTU), if available, is recommended as the first-line drug for treatment of hyperthyroidism during the first trimester of pregnancy because of the possible association of methimazole (MMI) with specific congenital abnormalities that occur during first trimester organogenesis. MMI may also be prescribed if PTU is not available or if a patient cannot tolerate or has an adverse response to PTU. Methimazole 10 mg is considered to be approximately equal to 100–150 mg of propylthiouracil. Recent analyses reported by the U.S. Food and Drug Administration (FDA) indicate that PTU may rarely be associated with severe liver toxicity. For this reason the Task Force recommends that clinicians change treatment of patients from PTU to MMI after the completion of the first trimester. Available data indicate that MMI and PTU are equally efficacious in treatment of pregnant women. Practitioners should use their clinical judgment in choosing the ATD therapy, including the potential difficulties involved in switching patients from one drug to another. If switching from PTU to MMI, thyroid function should be assessed after two weeks and then at two to four week intervals. (USPSTF Recommendation level: B, Evidence-fair) (1|++OO) Although liver toxicity may appear abruptly, it is reasonable to monitor liver function in pregnant women on PTU every three to four weeks and to encourage patients to promptly report any new symptoms. (USPSTF Recommendation level: C, Evidence-poor) (2|+OOO)

Subtotal thyroidectomy may be indicated during pregnancy as therapy for maternal Graves' disease if (i) a patient has a severe adverse reaction to ATD therapy, (ii) persistently high doses of ATD are required (over 30 mg/day of methimazole or 450 mg/day of PTU), or (iii) a patient is nonadherent to ATD therapy and has uncontrolled hyperthyroidism. The optimal timing of surgery is in the second trimester. (USPSTF Recommendation level C, Evidence-fair) (2|+OOO)

There is no evidence that treatment of subclinical hyperthyroidism improves pregnancy outcome, and treatment could potentially adversely affect fetal outcome. (USPSTF Recommendation level: C, Evidence-fair) (2|+OOO)

Management of Maternal Hyperthyroidism: Fetal Aspects

Since thyroid receptor antibodies (thyroid receptor stimulating, binding, or inhibiting antibodies) freely cross the placenta and can stimulate the fetal thyroid, these antibodies should be measured by 22 weeks gestational age in mothers with 1) current Graves' disease, or 2) a history of Graves' disease and treatment with ^{131}I or thyroidectomy before pregnancy, or 3) a previous neonate with Graves' disease, or 4) previously elevated TRAb. Women who have a negative TRAb and do not require ATD have a very low risk of fetal or neonatal thyroid dysfunction. (USPSTF Recommendation level: B, Evidence-fair) (1|+++O)

^{131}I should not be given to a woman who is or may be pregnant. If inadvertently treated, the patient should be promptly informed of the radiation danger to the fetus, including thyroid destruction if treated after the 12th week of gestation. (USPSTF Recommendation level: A, Evidence-good) (1|+++O) There are no data for or against recommending termination of pregnancy after ^{131}I exposure. (USPSTF Recommendation level: I, Evidence-poor) (2|+OOO)

In women with TRAb or thyroid stimulating immunoglobulin (TSI) elevated at least two- to three-fold the normal level, and in women treated with ATD, maternal free T_4 and fetal thyroid dysfunction should be screened for during the fetal anatomy ultrasound done in the 18th–22nd week and repeated every four to six weeks or as clinically indicated. Evidence of fetal thyroid dysfunction could include thyroid enlargement, growth restriction, hydrops, presence of goiter, advanced bone age, tachycardia or cardiac failure. If fetal hyperthyroidism is diagnosed and thought to endanger the pregnancy, treatment using MMI or PTU should be given with frequent clinical, laboratory and U.S. monitoring. (USPSTF Recommendation level: B, Evidence-fair) (1|+++O)

Umbilical blood sampling should be considered only if the diagnosis of fetal thyroid disease is not reasonably certain from the clinical and sonographic data, and the information gained would change the treatment. (USPSTF Recommendation level: B, Evidence-fair) (2|+OOO)

All newborns of mothers with Graves' disease (except those with negative TRAb and not requiring ATD) should be evaluated by a medical care provider for thyroid dysfunction and treated if necessary. (USPSTF Recommendation level: B, Evidence-fair) (1|+++O)

Gestational Hyperemesis and Hyperthyroidism

Thyroid function tests (TSH, total T_4 , or free T_4 index, or free T_4) and TRAb should be measured in patients with hyperemesis gravidarum (5% weight loss, dehydration, and ketonuria) and clinical features of hyperthyroidism. (USPSTF recommendation level: B; Evidence-fair) (2|++OO)

Most women with hyperemesis gravidarum, clinical hyperthyroidism, suppressed TSH, and elevated free T_4 do not require ATD treatment. (USPSTF recommendation level: A; Evidence-good) (1|+++++) Clinical judgment should be followed in women who appear significantly thyrotoxic or who have in addition serum total T_3 values above the reference range for pregnancy. Beta blockers such as metoprolol may be helpful and used with obstetrical agreement (USPSTF recommendation level: B; evidence-poor) (2|+OOO)

Women with hyperemesis gravidarum and diagnosed to have Graves' hyperthyroidism (free T_4 above the reference range or total T_4 >150% of top normal pregnancy value, TSH <0.01 $\mu\text{IU/L}$ and presence of TRAb) will require ATD treatment, as clinically necessary. (USPSTF recommendation level: A; evidence-good) (1|+++++)

Autoimmune Thyroid Disease and Miscarriage

A positive association exists between the presence of thyroid antibodies and pregnancy loss. Universal screening for antithyroid antibodies, and possible treatment, cannot be recommended at this time. As of January 2011, only one randomized interventional trial has suggested a decrease in the first trimester miscarriage rate in euthyroid antibody-positive women, but treatment duration was very brief before the outcome of interest. However, since women with elevated anti-TPO antibodies are at increased risk for progression of hypothyroidism, if identified such women should be screened for serum TSH abnormalities before pregnancy, as well as during the first and second trimesters of pregnancy. (USPSTF Recommendation level: C, Evidence-fair) (2|+OOO)

Thyroid Nodules and Cancer

Fine needle aspiration (FNA) cytology should be performed for predominantly solid thyroid nodules >1 cm discovered in pregnancy. Women with nodules 5 mm–1 cm in size should be considered for FNA if they have a high risk history or suspicious findings on ultrasound, and women with complex nodules 1.5–2 cm or larger should also receive an FNA. During the last weeks of pregnancy, FNA can reasonably be delayed until after delivery. Ultrasound-guided FNA is likely to have an advantage for maximizing adequate sampling. (USPSTF Recommendation level: B, Evidence-fair) (1|+++O)

When nodules discovered in the first or early second trimester are found to be malignant or highly suspicious on cytopathologic analysis, to exhibit rapid growth, or to be accompanied by pathologic neck adenopathy, pregnancy need not be interrupted, but surgery should be offered in the

second trimester. Women found to have cytology indicative of papillary cancer or follicular neoplasm without evidence of advanced disease, and who prefer to wait until the postpartum period for definitive surgery, may be reassured that most well-differentiated thyroid cancers are slow growing and that delaying surgical treatment soon after delivery is unlikely to change disease-specific survival. (USPSTF Recommendation level: B, Evidence-fair) (1|++OO)

It is appropriate to administer thyroid hormone to achieve a suppressed but detectable TSH in pregnant women with a previously treated thyroid cancer, in those with an FNA positive for or suspicious for cancer, or in those who elect to delay surgical treatment until postpartum. High risk patients may benefit more than low risk patients from a greater degree of TSH suppression. The free T₄ or total T₄ levels should ideally not be increased above the normal range for pregnancy. (USPSTF Recommendation level: I, Evidence-poor) (2|+OOO)

Radioactive iodine (RAI) with ¹³¹I should not be given to women who are breastfeeding or for at least four weeks after nursing has ceased. (USPSTF Recommendation level: A, Evidence-good) (1|++++) Furthermore, pregnancy should be avoided for six months to one year in women with thyroid cancer who receive therapeutic RAI doses to ensure stability of thyroid function and confirm remission of thyroid cancer. (USPSTF Recommendation level: B, Evidence-fair) (1|++OO)

Iodine Nutrition during Pregnancy

Women in childbearing age should have an average iodine intake of 150 µg per day. As long before pregnancy as possible, during pregnancy and breastfeeding, women should increase their daily iodine intake to 250 µg on average. (USPSTF Recommendation level: A, Evidence-good) (1|+++O)

Iodine intake during pregnancy and breastfeeding should not exceed twice the daily recommended nutrient intake (RNI) for iodine, i.e., 500 µg iodine per day. (USPSTF Recommendation level: I, Evidence-poor) (2|+OOO)

While not advised as a part of normal clinical practice, the adequacy of the iodine intake during pregnancy can be assessed by measuring urinary iodine concentration (UIC) in a representative cohort of the population. UIC should ideally range between 150 and 250 µg/L. If there is significant concern, the care-giver should assay TSH and thyroid hormone levels. (USPSTF Recommendation level: A, Evidence-good) (1|++++)

To reach the daily recommended nutrient intake for iodine, multiple means must be considered, tailored to the iodine intake level in a given population. Different situations must therefore be distinguished: a) countries with iodine sufficiency and/or with a well-established universal salt iodization (USI) program, b) countries without a USI program or with an established USI program where the coverage is known to be only partial, and c) remote areas with no accessible USI program and difficult socioeconomic conditions. (USPSTF Recommendation level: A, Evidence-good) (1|++++)

The Task Force recommends that once-daily prenatal vitamins contain 150–200 µg iodine and that this be in the form of potassium iodide or iodate, the content of which is verified to ensure that all pregnant women taking prenatal vitamins are protected from iodine deficiency. Ideally, supplementation should be started before conception. Preparations containing iron supplements should be separated from thyroid hormone administration by at least four hours (USPSTF Recommendation level: B, Evidence-fair) (2|++OO)

The Task Force recommends that breastfeeding women maintain a daily intake of 250 µg of iodine to ensure breast milk provides 100 µg iodine per day to the infant. (USPSTF Recommendation level: A, Evidence-good) (1|+++O)

Postpartum Thyroiditis

There are insufficient data to recommend screening of all women for postpartum thyroiditis (PPT). (USPSTF Recommendation level: I, Evidence-poor) (2|+OOO)

Women known to be TPO-Ab-positive should have a TSH performed at six to twelve weeks and at six months postpartum, or as clinically indicated. (USPSTF Recommendation level: A, Evidence-good) (1|+++O)

Because the prevalence of PPT in women with type 1 diabetes, Graves' disease in remission, and chronic viral hepatitis is greater than in the general population, screening by TSH is recommended at three and six months postpartum. (USPSTF Recommendation level: B, Evidence-fair) (2|++OO)

Women with a history of PPT have a markedly increased risk of developing permanent primary hypothyroidism in the five- to ten-year period following the episode of PPT. An annual TSH level should be performed in these women. (USPSTF Recommendation level: A, Evidence-good) (1|+++O)

Asymptomatic women with PPT who have a TSH above the reference range but less than 10 mIU/L and who are not planning a subsequent

pregnancy do not necessarily require intervention, but should, if untreated, be re-monitored in four to eight weeks. When a TSH above the reference range continues, women should be treated with levothyroxine. Symptomatic women and women with a TSH above normal and who are attempting pregnancy should be treated with levothyroxine. (USPSTF Recommendation level: B, Evidence-fair) (2|++OO)

There is insufficient evidence to conclude whether an association exists between postpartum depression (PPD) and either PPT or thyroid antibody positivity (in women who did not develop PPT). (USPSTF Recommendation level: I, Evidence-poor) (2|+OOO) However, as hypothyroidism is a potentially reversible cause of depression, women with PPD should be screened for hypothyroidism and appropriately treated. (USPSTF Recommendation level: B, Evidence-fair) (2|++OO)

Screening for Thyroid Dysfunction during Pregnancy

Universal screening of healthy women for thyroid dysfunction before pregnancy is not recommended. (USPSTF Recommendation level: I, Evidence-poor) (2|+OOO)

However, caregivers should identify individuals at 'high risk' for thyroid illness (Table 8, Section 8 in the original guideline) on the basis of their medical history, physical exam, or prior biochemical data. When such individuals are identified, prenatal measurement of serum TSH is recommended. If above 2.5 mIU/L, the test should be confirmed by repeat assay. While no RCTs are available to guide a response, the committee believes it is appropriate to give low-dose T₄ treatment to bring TSH below 2.5 mIU/L. This treatment can be discontinued if the woman does not become pregnant, or postpartum (USPSTF Recommendation level: I, Evidence-poor) (2|+OOO)

All women considering pregnancy with known thyroid dysfunction and receiving levothyroxine should be tested for abnormal TSH concentrations before pregnancy. (USPSTF Recommendation level: B, Evidence-fair) (1|++OO)

If hypothyroidism has been diagnosed before pregnancy, we recommend adjustment of the preconception thyroxine dose to reach prior to pregnancy a TSH level not higher than 2.5 mIU/L. (USPSTF Recommendation level: C, Evidence-fair) (2|++OO)

All women receiving levothyroxine should be verbally screened prenatally to assess their understanding of changing levothyroxine requirements following conception. These women should be counseled to contact a physician or medical professional immediately upon a missed menstrual cycle or suspicion of pregnancy to check their serum TSH level. An additional recommendation may be to increase their levothyroxine dose by 30%, which is often two additional tablets per week (nine tablets/week instead of seven tablets/week), until their serum TSH can be checked. (USPSTF Recommendation level: B, Evidence-fair) (2|++OO)

Universal screening for the presence of anti-TPO antibodies either before or during pregnancy is not recommended. (USPSTF Recommendation level: C, Evidence level-fair) (2|+OOO)

However, women with elevated anti-TPO antibodies are at increased risk for miscarriage, preterm delivery, progression of hypothyroidism, and PPT. Therefore, if identified, such women should be screened for serum TSH abnormalities before pregnancy, as well as during the first and second trimesters of pregnancy. (USPSTF Recommendation level: C, Evidence-fair) (1|++OO) (See also below.)

The committee could not reach agreement with regard to screening recommendations for all newly pregnant women. Two versions are therefore presented.

Some members recommended screening of all pregnant women for serum TSH abnormalities by the ninth week or at the time of their first visit. (USPSTF Recommendation level: C, Evidence-fair) (2|++OO)

Some members recommended neither for nor against universal screening of all pregnant women for TSH abnormalities at the time of their first visit. These members strongly support aggressive case finding to identify and test high-risk women (see Table 8, Section 8, in the original guideline document) for elevated TSH concentrations by the ninth week or at the time of their first visit before and during pregnancy, and recognize in some situations, ascertainment of the individual's risk status may not be feasible. In such cases, and where the local practice environment is appropriate, testing of all women by nine weeks of pregnancy or at the first prenatal visit is reasonable. (USPSTF Recommendation level: I, Evidence-poor) (2|+OOO)

If serum TSH is >2.5 mIU/L at the time of testing (or >3.0 mIU/L in the second trimester), levothyroxine therapy should be instituted. For overt hypothyroidism: (USPSTF Recommendation level: A, Evidence-good) (1|++++); for subclinical hypothyroidism and obstetrical outcome: (USPSTF Recommendation level: C, Evidence-fair) (2|+OOO); for subclinical hypothyroidism and neurological outcome: (USPSTF Recommendation level: C, Evidence level-poor) (2|+OOO)

If TSH concentration is 2.5–10 mIU/L, a starting levothyroxine dose of 50 mcg/day or more is recommended. Other thyroid preparations (such as triiodothyronine) are not recommended. (USPSTF Recommendation level: C, Evidence level-fair) (2|++OO)

Women at high-risk for PPT in the postpartum months should be screened via assessment of serum TSH. These high-risk groups include: 1) women known to be TPO-Ab+, 2) women with type 1 diabetes, and 3) women with a prior history of PPT. Screening should occur at six to twelve weeks postpartum. Women with Graves' disease who enter remission during pregnancy should be screened for recurrence by TSH assay at three to six months. (USPSTF Recommendation level: C, Evidence-poor) (2|+OOO) (See also "Postpartum Thyroiditis," above.)

Definitions:

Strength of Evidence

The United States Preventive Services Task Force (USPSTF) grades the overall evidence for a service on a three-point scale (good, fair, or poor):

Good: Evidence includes consistent results from well designed, well-conducted studies in representative populations that directly assess effects on health outcomes.

Fair: Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes.

Poor: Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

Strength of Recommendation

A: The USPSTF strongly recommends that clinicians provide (the service) to eligible patients. The USPSTF found good evidence that (the service) improves important health outcomes and concludes that benefits substantially outweigh harms.

B: The USPSTF recommends that clinicians provide (the service) to eligible patients. The USPSTF found at least fair evidence that (the service) improves important health outcomes and concludes that benefits outweigh harms.

C: The USPSTF makes no recommendation for or against routine provision of (the service). The USPSTF found at least fair evidence that (the service) can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.

D: The USPSTF recommends against routinely providing (the service) to asymptomatic patients. The USPSTF found good evidence that (the service) is ineffective or that harms outweigh benefits.

I: The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing (the service). Evidence that (the service) is effective is lacking, or poor quality, or conflicting, and the balance of benefits and harms cannot be determined.

Evidence Level by GRADE System

High: ++++

Moderate: +++O

Low: ++OO

Very Low: +OOO

Recommendation Level by GRADE System

1: Strong

2: Weak

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Thyroid dysfunction during pregnancy and postpartum including:

- Hypothyroidism
- Hyperthyroidism
- Gestational hyperemesis and hyperthyroidism
- Autoimmune thyroid disease
- Thyroid nodules and cancer
- Postpartum thyroiditis

Guideline Category

Management

Risk Assessment

Screening

Treatment

Clinical Specialty

Endocrinology

Family Practice

Internal Medicine

Obstetrics and Gynecology

Intended Users

Physicians

Guideline Objective(s)

- To update the guidelines for the management of thyroid dysfunction during pregnancy and postpartum published previously in 2007
- To provide clinical guidelines for the diagnosis, management and treatment of thyroid problems present just before and during pregnancy, and in the postpartum interval

Target Population

- Pregnant women and women who are postpartum with or at risk for thyroid dysfunction
- Women of childbearing potential

Interventions and Practices Considered

1. Testing and management of thyroxine (T_4) and thyroid-stimulating hormone (TSH) levels
2. Avoiding overt maternal hypothyroidism
3. Differential diagnosis of maternal hyperthyroidism and Graves' disease
4. Antithyroid drug therapy (propylthiouracil [PTU] or methimazole [MMI])

5. Subtotal thyroidectomy during pregnancy
6. Measurement of maternal and fetal thyroid receptor antibodies (thyroid receptor stimulating, binding, or inhibiting antibodies)
7. Avoiding ¹³¹I treatment in women who are or may be pregnant and in women who are breastfeeding or for at least four weeks after nursing has ceased
8. Screening for maternal free T₄ and fetal thyroid dysfunction during the fetal anatomy ultrasound
9. Treatment of fetal hyperthyroidism using MMI or PTU with frequent clinical, laboratory, and ultrasound monitoring
10. Umbilical blood sampling for diagnosis of fetal thyroid disease
11. Evaluation of newborns of mothers with Graves' disease for thyroid dysfunction and treatment if necessary
12. Beta-blockers such as metoprolol
13. Screening of women with elevated anti-thyroid peroxidase (TPO) antibodies for serum TSH abnormalities before pregnancy and during the first and second trimesters of pregnancy
14. Ultrasound-guided fine-needle aspiration (FNA) cytology for predominantly solid thyroid nodules
15. Surgery for thyroid cancer in the second trimester or in the postpartum period
16. Thyroid hormone administration to achieve a suppressed but detectable TSH
17. Maintaining adequate iodine intake in women in the childbearing age before pregnancy and during pregnancy and breastfeeding
18. Screening for postpartum thyroiditis (PPT) by TSH measurement in women with type 1 diabetes, Graves' disease in remission, and chronic viral hepatitis and those at this risk for PPT
19. Levothyroxine treatment and counseling about changing levothyroxine requirements after conception
20. Identification of individuals at "high risk" for thyroid illness and prenatal measurement of serum TSH

Note: The following were not recommended or has insufficient evidence for recommendation: treatment of subclinical hyperthyroidism, termination of pregnancy after ¹³¹I exposure, universal screening for antithyroid antibodies, screening of all women for postpartum thyroiditis (PPT), universal screening of healthy women for thyroid dysfunction before pregnancy, universal screening for the presence of anti-TPO antibodies either before or during pregnancy.

Major Outcomes Considered

- Risk for and prevalence of thyroid dysfunction in pregnancy and the postpartum period
- Incidence of fetal hyperthyroidism
- Incidence of miscarriage and preterm delivery
- Neuropsychological outcome of progeny
- Adverse effects of antithyroid drugs on fetal development and fetal thyroid

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

For the updated guideline, a literature search of PubMed was performed for the years 2001 through 2011. Multiple search terms were used at various times, but primarily consisted of PREGNANCY and THYROID DISEASE in order to start with the widest net. Searches were also performed on other terms, for example, THYROID CANCER, THYROIDITIS, MISCARRIAGE, HYPOTHYROIDISM, HYPERTHYROIDISM, SCREENING, etc. Articles were limited to English language studies in humans.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Rating Scheme for the Strength of the Evidence

The United States Preventive Services Task Force (USPSTF) grades the overall evidence for a service on a three-point scale (good, fair, or poor):

Good: Evidence includes consistent results from well designed, well conducted studies in representative populations that directly assess effects on health outcomes.

Fair: Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes.

Poor: Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

Level of Evidence by Grading of Recommendations Assessment, Development and Evaluation (GRADE) System

High: ++++

Moderate: +++O

Low: ++OO

Very Low: +OOO

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

The Task Force undertook to review all material on the guideline topics published in English during the past two decades, or earlier at the working group's discretion. They concentrated on original reports and largely excluded reviews from the references. Recently, reports of several prospective, randomized intervention trials have been published in this area, and the Task Force members are aware of large-scale prospective intervention trials that are ongoing. Nevertheless, in the last 20 years many high-quality studies have modified older dogmas and profoundly changed the ways in which these patients are managed. These studies are most often prospective or retrospective clinical evaluations of a particular patient population and matched groups of control women. Such studies, when carefully performed, adequately matched, and appropriately interpreted, provide much of the evidence presented in the guideline.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The Clinical Guidelines Subcommittee of The Endocrine Society deemed thyroid dysfunction during pregnancy a priority area in need of practice guidelines and appointed a Task Force to formulate evidence-based recommendations. An international Task Force was created under the auspices of The Endocrine Society to review the best evidence in the field and develop evidence-based guidelines, and a report was issued in 2007. Because of advances in the field, the committee was reconvened in 2009. The current Task Force also includes members of the Asia & Oceania Thyroid Association, European Thyroid Association, and the Latin American Thyroid Society.

The Task Force was composed of a chair selected by the Clinical Guidelines Subcommittee of The Endocrine Society, experts appointed by The

Endocrine Society, Asia & Oceania Thyroid Association, European Thyroid Association, and Latin American Thyroid Society, and a methodologist.

The Task Force followed the approach of the U.S. Preventive Services Task Force and the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system to evaluate the strength of each recommendation and the quality of the evidence. The Task Force used the best available research evidence to develop the recommendations.

In the USPSTF system, the strength of a recommendation is graded A, B, C, D, or I (if insufficient), and evidence is graded good, fair, or poor. In the GRADE system strong recommendations use the number 1, and weak recommendations use the number 2. The Task Force has confidence that persons who receive care according to the strong recommendations will derive, on average, more good than harm. Weak recommendations require more careful consideration of the person's circumstances, values, and preferences to determine the best course of action. Linked to each recommendation is a description of the evidence and the values that panelists considered in making the recommendation; in some instances, there are remarks, a section in which panelists offer technical suggestions for testing conditions, dosing, and monitoring. These technical comments reflect the best available evidence applied to a typical person being treated.

Consensus Process

The guideline was developed through a series of e-mails, conference calls, and one face-to-face meeting. An initial draft was prepared by the Task Force, with the help of a medical writer, and reviewed and commented on by members of The Endocrine Society, Asia & Oceania Thyroid Association, and the Latin American Thyroid Society. A second draft was reviewed and approved by The Endocrine Society Council. At each stage of review, the Task Force received written comments and incorporated substantive changes.

Rating Scheme for the Strength of the Recommendations

The United States Preventive Services Task Force (USPSTF) grades its recommendations (level A, B, C, D or I) on the basis of the strength of evidence and magnitude of net benefits (benefits minus harms):

A: The USPSTF strongly recommends that clinicians provide (the service) to eligible patients. The USPSTF found good evidence that (the service) improves important health outcomes and concludes that benefits substantially outweigh harms.

B: The USPSTF recommends that clinicians provide (the service) to eligible patients. The USPSTF found at least fair evidence that (the service) improves important health outcomes and concludes that benefits outweigh harms.

C: The USPSTF makes no recommendation for or against routine provision of (the service). The USPSTF found at least fair evidence that (the service) can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.

D: The USPSTF recommends against routinely providing (the service) to asymptomatic patients. The USPSTF found good evidence that (the service) is ineffective or that harms outweigh benefits.

I: The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing (the service). Evidence that (the service) is effective is lacking, or poor quality, or conflicting, and the balance of benefits and harms cannot be determined.

Recommendation Level by Grading of Recommendations Assessment, Development, and Evaluation (GRADE) System

1: Strong

2: Weak

Note: There are no equivalents in the GRADE system for the recommendation levels C, D, and I used in the USPSTF system.

Cost Analysis

A formal cost analysis was not performed but published cost analyses were reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

An initial draft was reviewed and commented on by members of The Endocrine Society, Asia & Oceania Thyroid Association, and the Latin American Thyroid Society. A second draft was reviewed and approved by The Endocrine Society Council. At each stage of review, the Task Force received written comments and incorporated substantive changes.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is specifically stated for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis and management of thyroid dysfunction during pregnancy and postpartum

Potential Harms

- Overtreatment of the mother with thioamides can result in iatrogenic fetal hypothyroidism, but undertreatment of maternal hyperthyroidism may lead to central congenital hypothyroidism.
- Recent analyses reported by the U.S. Food and Drug Administration (FDA) indicate that propylthiouracil (PTU) may rarely be associated with severe liver toxicity. For this reason it is recommended that clinicians change treatment of patients from PTU to methimazole (MMI) after the completion of the first trimester. MMI can also damage the liver, but this damage is characterized by a cholestatic picture rather than the hepatocellular injury associated with PTU.
- Treatment of maternal subclinical hyperthyroidism has not been found to improve pregnancy outcome and may risk unnecessary exposure of the fetus to antithyroid drugs (ATDs).
- ATDs are associated with side effects such as agranulocytosis.
- There have been reports of two distinct teratogenic patterns associated with MMI: aplasia cutis and choanal/esophageal atresia. The data supporting these associations are controversial.
- Use of propranolol in late pregnancy has been associated with mild and transitory neonatal hypoglycemia, apnea, and bradycardia. There are case reports suggesting an association between propranolol use and intrauterine growth restriction, but this remains controversial.
- Fetal exposure to high doses of radiation before organogenesis (before 4 to 6 weeks gestation) can lead to miscarriage or have no effect. Radiation exposure later in gestation can be associated with malformations, growth restriction, developmental delay and induction of malignancies. However, the likelihood of these effects is not certain. Exposure after 12 weeks can induce thyroid ablation, requiring intrauterine thyroid hormone replacement and lifelong therapy for hypothyroidism.
- If surgery is elected in pregnancy, it is best avoided in the first and third trimesters. During the first trimester, there is concern over the possible teratogenic effects on the fetus, and surgery of any type is associated with increased early fetal loss. Surgery of any type in the third trimester is associated with a higher incidence of preterm labor. For cancer found early in pregnancy, surgery during the second trimester before fetal viability (before 22 weeks) appears safest for the patient and the fetus. Fetal loss has been reported only in association with extensive neck exploration.

Contraindications

Contraindications

- Radioactive iodine (RAI) diagnostic tests and therapy are contraindicated during pregnancy, and all women who could potentially become

pregnant should have a pregnancy test prior to ¹³¹I administration.

- ¹³¹I is contraindicated in breastfeeding mothers, and breastfeeding should cease if the exposure is unavoidable.
- Radionuclide scanning of the thyroid is contraindicated during pregnancy.

Qualifying Statements

Qualifying Statements

- Clinical Practice Guidelines are developed to be of assistance to endocrinologists and other health care professionals by providing guidance and recommendations for particular areas of practice. The Guidelines should not be considered inclusive of all proper approaches or methods, or exclusive of others. The Guidelines cannot guarantee any specific outcome, nor do they establish a standard of care. The Guidelines are not intended to dictate the treatment of a particular patient. Treatment decisions must be made based on the independent judgment of health care providers and each patient's individual circumstances.
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Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Foreign Language Translations

Patient Resources

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

The Endocrine Society. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. Chevy Chase (MD): The Endocrine Society; 2012. 99 p. [387 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2007 (revised 2012)

Guideline Developer(s)

The Endocrine Society - Professional Association

Source(s) of Funding

The Endocrine Society

Guideline Committee

Thyroid Dysfunction during Pregnancy and Postpartum Guideline Task Force

Composition of Group That Authored the Guideline

Authors: Leslie De Groot, MD; Marcos Abalovich, MD; Erik K Alexander, MD; Nobuyuki Amino, MD; Linda Barbour, MD; Rhoda Cobin, MD; Creswell Eastman, MD; John Lazarus, MD; Dominique Luton, MD; Susan Mandel, MD; Jorge Mestman, MD; Joanne Rovet, MD; Scott Sullivan, MD

Financial Disclosures/Conflicts of Interest

Leslie De Groot, MD (chair)—Financial or Business/Organizational Interests: none disclosed; Significant Financial Interest or Leadership Position: none disclosed.

Marcos Abalovich, MD—Financial or Business/Organizational Interests: American Thyroid Association Thyroid and Pregnancy Guidelines Task Force; Significant Financial Interest or Leadership: none disclosed.

Erik K. Alexander, MD—Financial or Business/Organizational Interests: Veracyte, Inc.; Significant Financial Interest or Leadership Position: none disclosed.

Nobuyuki Amino, MD—Financial or Business/Organizational Interests: none disclosed; Significant Financial Interest or Leadership: none disclosed.

Linda Barbour, MD, MSPH—Financial or Business/Organizational Interests: none disclosed; Significant Financial Interest or Leadership Position: none disclosed.

Rhoda Cobin, MD—Financial or Business/Organizational Interests: none disclosed; Significant Financial Interest or Leadership Position: none disclosed.

Creswell Eastman, MD—Financial or Business/Organizational Interests: International Council on Iodine Deficiency and Disorders; Significant Financial Interest or Leadership Position: none disclosed.

John Lazarus, MD—Financial or Business/Organizational Interests: British Thyroid Foundation, Abbott Labs, Merck-Serono; Significant Financial Interest or Leadership Position: none disclosed.

Dominique Luton, MD—Financial or Business/Organizational Interests: none disclosed; Significant Financial Interest or Leadership Position: none disclosed.

Susan Mandel, MD—Financial or Business/Organizational Interests: American Association of Clinical Endocrinology, American Thyroid Association, Association of Program Directors in Endocrinology, Diabetes and Metabolism; Significant Financial Interest or Leadership Position: none disclosed.

Jorge Mestman, MD—Financial or Business/Organizational Interests: American Thyroid Association; Significant Financial Interest or Leadership Position: none disclosed.

Joanne Rovet, PhD—Financial or Business/Organizational Interests: American Thyroid Association, Pediatric Endocrine Society; Significant Financial Interest or Leadership Position: none disclosed.

Scott Sullivan, MD—Financial or Business/Organizational Interests: American Thyroid Association, American College of Gynecology; Significant Financial Interest or Leadership Position: none disclosed.

Guideline Endorser(s)

Asian & Oceania Thyroid Association - Disease Specific Society

European Thyroid Association - Disease Specific Society

Latin American Thyroid Society - Disease Specific Society

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: The Endocrine Society. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. Chevy Chase (MD): The Endocrine Society; 2007. 79 p.

Guideline Availability

Electronic copies: Available for purchase from [The Endocrine Society Web site](#) .

Print copies: Available from The Endocrine Society, Phone: (301) 941.0210; Email: SocietyServices@endo-society.org

Availability of Companion Documents

The following is available:

- Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. Executive summary. 2012. 33 p. Electronic copies: Available in Portable Document Format (PDF) from [The Endocrine Society Web site](#) .

Patient Resources

The following are available:

- Detecting and treating thyroid nodules and cancer before, during, and after pregnancy: a patient's guide. 2012 Nov. 2 p. Electronic copies: Available from [The Hormone Foundation Web site](#) .
- Patient guide to detecting and treating hyperthyroidism before, during and after pregnancy. 2012 Aug. 2 p. Electronic copies: Available from [The Hormone Foundation Web site](#) .
- Patient guide to detecting and treating hypothyroidism before, during and after pregnancy. 2012 Oct. 2 p. Electronic copies: Available from [The Hormone Foundation Web site](#) .
- Congenital hypothyroidism fact sheet. 2012 Mar. 2 p. Electronic copies: Available from [The Hormone Foundation Web site](#) .
- Medicines for hypothyroidism fact sheet. 2011 Jul. 2 p. Electronic copies: Available in [English](#) and [Spanish](#) from The Hormone Foundation Web site.
- Postpartum thyroiditis fact sheet. 2012 Jan. 2 p. Electronic copies: Available in PDF in [English](#) and [Spanish](#) from The Hormone Foundation Web site.
- Radioactive iodine treatment for hyperthyroidism fact sheet. 2012 Apr. 2 p. Electronic copies: Available from [The Hormone Foundation Web site](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on November 1, 2007. The information was verified by the guideline developer on December 10, 2007. This summary was updated by ECRI Institute on June 15, 2009 following the FDA advisory on Propylthiouracil (PTU). This summary was updated by ECRI Institute on May 27, 2010 following the revised FDA advisory on Propylthiouracil (PTU). This summary was updated by ECRI Institute on January 25, 2013. The updated information was verified by the guideline developer on February 11, 2013.

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